

WHAT IS CLAIMED IS:

1. An isolated polynucleotide encoding a myocardin polypeptide.
2. The isolated polynucleotide of claim 1, wherein the myocardin polypeptide comprises an amino acid sequence of SEQ ID NO:2, SEQ ID NO:26, SEQ ID NO:28, or SEQ ID NO:30.
3. The isolated polynucleotide of claim 2, wherein the polynucleotide sequence comprises SEQ ID NO:1, SEQ ID NO:25, SEQ ID NO:27 or SEQ ID NO:29.
4. The polynucleotide of claim 1, wherein said polynucleotide further comprises a promoter operable in eukaryotic cells.
5. An isolated nucleic acid segment comprising at least 15 contiguous nucleotides of SEQ ID NO:1, SEQ ID NO:25, SEQ ID NO:27 or SEQ ID NO:29.
6. The isolated nucleic acid segment of claim 5, wherein said segment is 15 nucleotides in length.
7. The isolated nucleic acid segment of claim 5, wherein said segment is 20 nucleotides in length.
8. The isolated nucleic acid segment of claim 5, wherein said segment is 25 nucleotides in length.
9. The isolated nucleic acid segment of claim 5, wherein said segment is 30 nucleotides in length.
10. The isolated nucleic acid segment of claim 5, wherein said segment is 35 nucleotides in length.
11. The isolated nucleic acid segment of claim 5, wherein said segment is 50 nucleotides in length.

12. The isolated nucleic acid segment of claim 5, wherein said segment is 100 nucleotides in length.
13. The isolated nucleic acid segment of claim 5, wherein said segment is 150 nucleotides in length.
- 5 14. The isolated nucleic acid segment of claim 5, wherein said segment is 250 nucleotides in length.
15. The isolated nucleic acid segment of claim 5, wherein said segment is 500 nucleotides in length.
16. The isolated nucleic acid segment of claim 5, wherein said segment is 1000 nucleotides in length.
17. The isolated nucleic acid segment of claim 5, wherein said segment is 2000 nucleotides in length.
18. The isolated nucleic acid segment of claim 5, wherein the number of contiguous nucleotides is 20.
- 15 19. The isolated nucleic acid segment of claim 5, wherein the number of contiguous nucleotides is 25.
20. The isolated nucleic acid segment of claim 5, wherein the number of contiguous nucleotides is 30.
- 20 21. The isolated nucleic acid segment of claim 5, wherein the number of contiguous nucleotides is 35.
22. The isolated nucleic acid segment of claim 5, wherein the number of contiguous nucleotides is 50.
23. An expression cassette comprising a polynucleotide encoding a myocardin polypeptide operably linked to a regulatory sequence.

24. The expression cassette of claim 23, wherein the polynucleotide encodes a polypeptide having an amino acid sequence of SEQ ID NO:2, SEQ ID NO:26, SEQ ID NO:28 or SEQ ID NO:30.
25. The expression cassette of claim 24, wherein the polynucleotide sequence comprises SEQ ID NO:1, SEQ ID NO:25, SEQ ID NO:27 or SEQ ID NO:29.
26. The expression cassette of claim 23, wherein said regulatory sequence comprises a promoter heterologous to the coding sequence.
27. The expression cassette of claim 26, wherein said promoter is a tissue specific promoter.
28. The expression cassette of claim 27, wherein said promoter is a muscle specific promoter.
29. The expression cassette of claim 28, wherein said muscle specific promoter is myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, creatine kinase promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter or atrial natriuretic factor promoter.
30. The expression cassette of claim 28, wherein said muscle specific promoter is a cardiac muscle specific promoter.
31. The expression cassette of claim 30, wherein said cardiac muscle specific promoter is α -myosin heavy chain or ANF.
32. The expression cassette of claim 23, wherein said promoter is an inducible promoter.
33. The expression cassette of claim 23, wherein said promoter is a constitutive promoter.

34. The expression cassette of claim 23, wherein said expression cassette is contained in a gene delivery vector.
35. The expression cassette of claim 34, wherein said gene delivery vector is a viral vector.
- 5 36. The expression cassette of claim 35, wherein said viral vector is a retroviral vector, an adenoviral vector, an adeno-associated viral vector, a vaccinia viral vector, a herpesviral vector, a polyoma viral construct or a Sindbis viral vector.
37. The expression cassette of claim 23, wherein said expression cassette further comprises a polyadenylation signal.
- 10 38. The expression cassette of claim 23, wherein said expression cassette further comprises a second polynucleotide encoding a second polypeptide.
39. The expression cassette of claim 38, wherein said second polypeptide is a cardiac transcription factor.
- 15 40. A transformed host cell comprising a polynucleotide encoding a myocardin polypeptide and a promoter heterologous to the polypeptide coding region, wherein said promoter directs expression of said myocardin polypeptide.
41. The transformed host cell of claim 40, further defined as a prokaryotic host cell.
42. The transformed host cell of claim 40, further defined as an eukaryotic host cell.
- 20 43. A method of using a host cell comprising an expression cassette comprising a polynucleotide encoding a myocardin polypeptide and a promoter active in said host cell comprising culturing the host cell under conditions suitable for the expression of the myocardin polypeptide.
44. A peptide of 8 to about 50 residues comprising at least 8 consecutive residues of SEQ ID NO:2, SEQ ID NO:26, SEQ ID NO:28 or SEQ ID NO:30.

45. The peptide of claim 44, wherein said peptide comprises 10 consecutive residues of SEQ ID NO:2, SEQ ID NO:26, SEQ ID NO:28 or SEQ ID NO:30.
46. The peptide of claim 44, wherein said peptide comprises 12 consecutive residues of SEQ ID NO:2, SEQ ID NO:26, SEQ ID NO:28 or SEQ ID NO:30.
47. A fusion protein comprising a myocardin protein or peptide fused to a second protein or peptide.
48. A method of modulating the phenotype of a non-cardiomyocyte cell to include one or more phenotypic functions of a cardiomyocyte cell comprising introducing into said non-cardiac cell an expression cassette comprising a polynucleotide encoding a myocardin polypeptide and a promoter active in said non-cardiac cell, wherein said promoter directs the expression of said polypeptide.
49. The method of claim 48, wherein said non-cardiomyocyte cell is a fibroblast.
50. The method of claim 48, wherein said method further comprises measuring cardiac lineage markers.
51. The method of claim 48, wherein said expression cassette further comprises a second polynucleotide encoding a second polypeptide.
52. The method of claim 51, wherein said second polypeptide is a cardiac transcription factor.
53. The method of claim 52, wherein said cardiac transcription factor is GATA4.
54. The method of claim 51, wherein said second polynucleotide is under the control of a second promoter.
55. The method of claim 51, wherein said first and second polynucleotide are the under control of the same promoter.
56. The method of claim 48, wherein said method further comprises introducing a second expression cassette into said non-cardiomyocyte cells, wherein said

second expression cassette comprises a polynucleotide encoding a second polypeptide and a second promoter active in said non-cardiomyocyte cells, wherein said second promoter directs the expression of said second polypeptide.

57. The method of claim 50, wherein measuring comprises RNA hybridization.
58. The method of claim 50, wherein measuring comprises PCR.
59. The method of claim 50, wherein measuring comprises RT-PCR.
60. The method of claim 50, wherein measuring comprises Western analysis.
61. A method of generating a cardiomyocyte comprising introducing into a cardiac fibroblast an expression vector comprising a polynucleotide encoding a myocardin polypeptide and a promoter active in said fibroblast, wherein said promoter directs the expression of said polypeptide.
62. The method of claim 61, wherein said expression vector comprises a lipid-based vector.
63. The method of claim 61, wherein said expression vector comprises a viral vector.
64. The method of claim 63, wherein said viral vector is a retroviral vector, an adenoviral vector, an adeno-associated viral vector, a vaccinia viral vector, a herpesviral vector, a polyoma viral construct or a Sindbis viral vector.
65. The method of claim 61, wherein said promoter is heterologous to the coding sequence.
66. The method of claim 61, wherein said promoter is a tissue specific promoter.
67. The method of claim 66, wherein said promoter is a muscle specific promoter.
68. The method of claim 67, wherein said muscle specific promoter is a cardiac muscle specific promoter.

69. The method of claim 61, wherein said expression cassette further comprises a second polynucleotide encoding a second polypeptide.
70. The method of claim 69, wherein said second polypeptide is a cardiac transcription factor.
- 5 71. The method of claim 70, wherein said cardiac transcription factor is GATA4.
72. The method of claim 69, wherein said second polynucleotide is under the control of a second promoter active in a cardiac fibroblast.
73. The method of claim 69, wherein said first and second polynucleotide are under the control of the same promoter.
- 10 74. The method of claim 61, wherein said method further comprises introducing into said fibroblasts a said second expression cassette comprising a polynucleotide encoding a second polypeptide and a second promoter active in said fibroblast, wherein said second promoter directs the expression of said second polypeptide.
- 15 75. The method of claim 61, wherein said expression cassette further comprises a polyadenylation site.
76. The method of claim 61, wherein said expression cassette further comprises a selectable marker.
77. The method of claim 76, wherein said selectable marker is an immunologic marker.
- 20 78. A method of stimulating cardiac tissue regeneration comprising inhibiting the function of myocardin in a post-mitotic cardiomyocyte.
79. The method of claim 78, wherein inhibiting comprises providing to said post-mitotic cardiomyocyte an antisense nucleic acid that inhibits transcription or translation of a myocardin mRNA.

80. The method of claim 79, wherein providing comprises introducing into said post-mitotic cardiomyocyte an expression cassette encoding myocardin antisense RNA and a promoter active in said cardiomyocytes.
81. A method of expressing a myocardin polypeptide in a host cell comprising introducing into said host cells an expression vector comprising a polynucleotide encoding a myocardin polypeptide, said polynucleotide being positioned under control of a promoter operable in said host cell.
82. A monoclonal antibody that binds immunologically to a polypeptide comprising SEQ ID NO:2, SEQ ID NO:26, SEQ ID NO:28 or SEQ ID NO:30 or an antigenic fragment thereof.
83. A polyclonal antisera, antibodies of which bind immunologically to a polypeptide comprising SEQ ID NO:2, SEQ ID NO:26, SEQ ID NO:28 or SEQ ID NO:30 or an antigenic fragment thereof.
84. A hybridoma cell that produces a monoclonal antibody that binds immunologically to a polypeptide comprising SEQ ID NO:2, SEQ ID NO:26, SEQ ID NO:28 or SEQ ID NO:30 or an antigenic fragment thereof.
85. A non-human transgenic animal comprising an expression cassette, wherein said expression cassette comprises a polynucleotide encoding a myocardin peptide or protein and a promoter operable in eukaryotic cells, said promoter being heterologous to the myocardin peptide or protein encoding region.
86. The animal of claim 85, wherein said expression cassette further comprises a selectable marker.
87. The animal of claim 85, wherein said promoter is constitutive.
88. The animal of claim 85, wherein said promoter is tissue specific.
89. The animal of claim 85, wherein said promoter is inducible.

90. The animal of claim 85, wherein said animal is a mouse.
91. A non-human transgenic animal comprising a defective germ-line myocardin allele.
92. The non-human transgenic animal of claim 91, comprising two defective germ-line myocardin alleles.
93. A method of treating a heart disease, including cardiomyopathy comprising administering to an animal suffering therefrom an expression cassette comprising a polynucleotide encoding a myocardin peptide or protein and a promoter operable in eukaryotic cells.
94. The method of claim 93, wherein said cardiomyopathy is myocardial infarction or hypertension.
95. The method of claim 93, wherein said promoter is a cardiac specific promoter.
96. The method of claim 93, wherein said expression cassette is comprised within a replication-defective expression vector.
97. The method of claim 96, wherein said replication defective expression vector is a viral vector.
98. The method of claim 97, wherein said viral vector is a retroviral vector, an adenoviral vector, an adeno-associated viral vector, a vaccinia viral vector, a herpesviral vector, a polyoma viral construct or a Sindbis viral vector.
99. A method of treating a heart disease, including cardiomyopathy comprising the step of providing to an animal suffering therefrom a myocardin antisense nucleic acid.
100. A method of decreasing mortality in a subject with heart failure comprising inhibiting the function of myocardin in post-mitotic cardiomyocytes in the subject.

101. A method of decreasing mortality in a subject with heart failure comprising increasing the level of myocardin in fibroblasts to generate cardiomyocytes in the subject.

102. A method of decreasing morbidity in a subject with heart failure comprising inhibiting the function of myocardin in post-mitotic cardiomyocytes in the subject.

103. A method of decreasing morbidity in a subject with heart failure comprising increasing the level of myocardin in fibroblasts to generate cardiomyocytes in the subject.

104. A method of screening for a candidate substance for an effect on myocardin regulation of cardiomyocyte development comprising:

- (a) providing myocardin and GATA to a cell;
- (b) admixing myocardin and GATA in the presence of said candidate substance; and
- (c) measuring the effect of said candidate substance on the expression of a cardiac lineage marker,

wherein a difference in the expression of said cardiac lineage marker, as compared to an untreated cell, indicates that said candidate substance effects myocardin regulation of cardiomyocyte development.

105. The method of claim 104, wherein measuring comprises RNA hybridization.

106. The method of claim 104, wherein measuring comprises PCR.

107. The method of claim 104, wherein measuring comprises RT-PCR.

108. The method of claim 104, wherein measuring comprises immunologic detection of myocardin.

109. The method of claim 104, wherein measuring comprises ELISA.
110. The method of claim 104, wherein measuring comprises immunohistochemistry.
111. The method of claim 104, wherein said cell is located in an animal.
112. The method of claim 104, wherein said cell is a fibroblast.
- 5 113. The method of claim 104, wherein said cell is a cardiomyocyte.
114. The method of claim 104, wherein said cardiac lineage marker is Nkx2.5.
115. The method of claim 104, wherein said modulator increases the expression of said cardiac lineage marker.
116. The method of claim 104, wherein said modulator decreases the expression of said cardiac lineage marker.
117. A method of screening for a modulator of myocardin expression comprising:
- (a) providing a cell that expresses a myocardin polypeptide;
 - (b) contacting said myocardin polypeptide with a candidate substance; and
 - (c) measuring the expression of myocardin,
- 15 wherein a difference in myocardin expression, indicates that said candidate substance is a modulator of myocardin expression.
118. The method of claim 117, wherein said modulator enhances myocardin expression.
119. The method of claim 117, wherein said modulator inhibits myocardin expression.
- 20 120. The method of claim 117, wherein said candidate modulator is a pharmaceutical composition.

121. A method of screening a candidate substance for myocardin binding activity comprising:

- (a) providing a myocardin polypeptide;
- (b) contacting the myocardin polypeptide with the candidate substance; and
- (c) determining the binding of the candidate substance to the myocardin polypeptide.

122. The method of claim 121, wherein the assay is performed in a cell free system.

123. The method of claim 121, wherein the assay is performed in a cell.

124. The method of claim 121, wherein the assay is performed *in vivo*.

125. The method of claim 121, wherein said candidate substance is an inhibitor of myocardin.

126. The method of claim 121, wherein said candidate substance is an enhancer of myocardin.